

GERMAN SCIENCE

Board Protest Stops a Shake-Up of the Dahlem Conferences

BERLIN—A crisis over the future of the prestigious Dahlem Conferences in Berlin that was brewing into a major furor has been calmed—at least for now. On 14 February, president Dieter Lenzen of the Free University in Berlin, which administers the conferences, agreed to reinstate a staff member whom the administration had dismissed and to protect the meetings from outside meddling with the scientific agenda.

Lenzen took these steps after he received a letter from members of Dahlem's scientific advisory board charging that the university was damaging the scientific reputation of the meetings and announcing their decision to resign. Several had said they would try to reestablish the conferences outside the university. But Lenzen's last-minute change of heart appears to have mollified at least some of the critics, who say they will give the university another chance.

The Dahlem conferences, named for the West Berlin neighborhood of villas and leafy boulevards where the conferences are held, were founded in 1974 as a way to boost the divided city's scientific reputation. Two or three conferences are held per year on broad topics such as "Genetic and Cultural Evolution of Cooperation" and "The Dynamics of Fault Zones." During the weeklong, invitation-only sessions, roughly 40 participants break into working groups to discuss position papers—often drafted to be as provocative as possible—and prepare a synthesis statement to be presented on the final day. The proceedings are published in book format.

More than 4000 scientists from around the world have taken part in 95 conferences over the past 3 decades. Fans of Dahlem say it offers a unique approach to tackling problems and making interdisciplinary connections. "The Dahlem format is such a great alternative" to the standard conference design, says Gerd Gigerenzer of the Max Planck Institute for Human Development in Berlin, who has led two Dahlem workshops.

In recent months scientists involved with the conferences charged that the university was undermining their scientific integrity. Specifically, they claimed that members of an International Advisory Board, established in 2003 to raise funds for the meetings, were attending scientific planning meetings uninvited and that the administration had pressured organizers to highlight Free University researchers instead of international experts in the lineup of participants. In early November, administration officials removed the long-time coordinator of the conferences, Julia



Back from the brink. A feud over Dahlem's leadership has calmed.

Lupp, from her position and forbade her from speaking to anyone connected to the conferences. They said she was on sick leave.

Members of the scientific advisory board protested that the administration should have consulted them about such an important staffing change and that Lupp had done nothing to deserve firing. In January, an inquiry by a board member and the university found no fault in Lupp's job perform-

ance, but the administration refused to reconsider its decision.

By mid-February, nearly half of the advisory board had decided to resign, and organizers of three planned conferences had withdrawn their proposals and were looking for new venues. The international outcry apparently had an effect. Lenzen agreed on 14 February to reinstate Lupp and to draw up new guidelines to protect the science from fundraising or other pressures.

Observers say they are cautiously optimistic about Dahlem's future. Eörs Szathmáry of the Institute for Advanced Study in Budapest, who has been coordinating a conference scheduled for May, says he would reconsider his decision to withdraw the workshop if he received "an official, written" letter from the university confirming Lupp's reinstatement and "guaranteeing protection from nonacademic influences." Gigerenzer says he hoped the university would follow through on its promises. "The first Dahlem conference was one of the best I've ever organized," Gigerenzer says. "If the conflict is solved, that is good news."

—GRETCHEN VOGEL

BIOCHEMISTRY

Irresistible Lure for Cockroaches Determined

In search of mates, frogs croak, birds sing, and cockroaches wear their own special perfume. For almost 10 years, researchers have tried to decipher the chemical formula of the male-luring scent emitted by female German cockroaches. Now that formula is finally in hand. As a result, city dwellers may one day be less squeamish about turning on the light at night: The chemical may result in a "very powerful system" for pest control, says Walter Leal, a chemical ecologist at the University of California, Davis.

On page 1104, Satoshi Nojima, a chemist now at the Shin-Etsu Chemical Co. in Tokyo,

Japan, and his colleagues describe the arduous path they took to characterize this chemical, one of several pheromones produced by cockroaches. They also show that a synthetic version of it is a potent attractant for the insects. "It was very difficult to do, very time-consuming," says Robert Kopanic Jr., an entomologist at S. C. Johnson and Son Inc. in Racine, Wisconsin.

German cockroaches are the bane of urban residents. As many as 100,000 can live in a single apartment or house; baits and sticky traps are only moderately effective, and insecticides are not environmental friendly.

So it was exciting news when Coby Schal, an urban entomologist at North Carolina State University in Raleigh, and Dangsheng Laing, now at Atex Bait Co. in Santa Clara, California, reported in 1993 that female cockroaches gave off a volatile compound, or pheromone, that attracts males from meters away. But taking the next step, identifying the pheromone, proved almost impossible. "Every time [we] tried to isolate it, it fell apart," recalls Wendell Roelofs, a ▶



Love is blind. A synthetic version of the female scent that attracts males (on female's back) may help with cockroach control.

biochemist at the New York State Agricultural Experiment Station in Geneva.

Adding to the challenge, females produce so little pheromone that researchers needed to dissect 15,000 of them, removing the pheromone-producing gland from each, to extract enough material for analysis. And Nojima—who was working with Roelofs at the time—had to come up with new ways to pin down the attractant among the many compounds in the extracts.

Nojima joined a single detached cockroach antenna to electrodes and exposed it to the chemicals exiting a gas chromatograph, which had separated the roach extract into discrete components. If the antenna sent a

signal to the electrodes, he knew he had a good candidate pheromone. The night before he flew back to Japan—his postdoc was ending—Nojima struck cockroach gold when his system recorded a hit. “After 10 years of work, it came down to one night,” says Schal.

Fran Webster of Syracuse University in New York found that the newly isolated compound, called blattellaquinone after the cockroach’s Latin name *Blattella*, has a novel structure. But it is similar enough to a commercial product that it is relatively inexpensive to synthesize. The compound clearly attracts male roaches: They prefer the dissolved synthetic pheromone over a control solvent about 93% of the time, on par with

their preferences for the natural pheromone. Moreover, field tests at a cockroach-infested pig farm indicate that many males can’t resist the synthetic version.

If the compound proves to be effective over long periods, it could be quite useful for pest control, says Kopanic. Even though blattellaquinone only attracts males, they are the wanderers among the two sexes. The new pheromone should lure males into traps or to poison laced with the compound. In the latter case, they would then transfer the poison, through their feces, to females and their young, suggests Schal. If so, for male roaches, the female scent may one day lead to poison, not procreation. —ELIZABETH PENNISI

AGRICULTURAL RESEARCH

Ag Schools Say They Can't Afford Budget Boost

Agricultural researchers have long been green with envy at the budgets of U.S. research agencies that fund their colleagues in other disciplines. So President George W. Bush’s request last week for a 39% increase in the U.S. Department of Agriculture’s (USDA’s) signature competitive grants program would seem to be cause for celebration. Instead, university lobbyists have declared war on the proposal because it siphons money from a different program that assured some schools steady funding for infrastructure, salaries, and research on local problems.

At issue is the Administration’s 2006 budget request for \$250 million for the National Research Initiative (NRI). USDA officials say it will improve accountability and yield big dividends for agriculture. “We know that competitive grants usually bring out the better science,” says Joseph Jen, USDA’s undersecretary for research, education, and economics. USDA also wants to remove a mandated cap on the amount of overhead that institutions can receive for the cost of supporting federally funded research.

A larger NRI, Jen says, would include more research on obesity prevention and agricultural biosecurity, such as applying genomics to develop better diagnostic tests for animal and crop disease. That’s an appealing vision, especially to officials at larger schools. “It’s a good move,” comments Peter Barry, director of the Center for Farm and Rural Business Finance at the University of Illinois, Urbana-Champaign. “Increased funding will take the program to a new level and significantly extend its capacity to address major societal problems.”

Universities don’t object to the boost for NRI, which has never come close to being the half-billion-dollar-a-year program recommended in a 1994 report from the National Academy of Sciences. But the 2006 request, they complain, takes a knife to a \$550-million-a-year pot that funds agricultural experiment stations at so-called Land-

national competitive grants” for such applied research, says Marc Johnson, dean of the College of Agricultural Sciences at Colorado State. Without another source of funding, Johnson and other deans say they will be forced to end applied research and shrink graduate programs.

Another concern is that the cut in formula funds will hurt infrastructure, such as greenhouses and herds of research animals. “Grant agencies in the past have not liked funding facilities,” says Fretz. But these expenses are no less real, he notes: “You can’t have breaks in funding and maintain a dairy herd.”

To soften the blow, USDA has proposed fencing off \$75 million for a competition among land-grant colleges. But department officials are still working out the details, leading to concern that these competitive grants won’t be awarded in time to replace the cut in formula funding. “That will leave a pretty big hole for the year,” says Johnson.

The next step is up to Congress, and lobbyists are already gearing up. “Our number one priority is to reinstate the formula funds,” says Fred Cholick, dean of the College of Agriculture at Kansas State University and chair of the agriculture budget and advocacy committee for the National Association of State Universities and Land-Grant Colleges. Even advocates for NRI doubt that the president will get all that he wants. “I can’t see [legislators] giving up their earmarks,” says Karl Glasener, who tracks federal agricultural policy for three scientific societies.

—AMITABH AVASTHI AND ERIK STOKSTAD



Plucked? Researchers worry that poultry flocks, livestock herds, and other research infrastructure, such as greenhouses, might be cut.

Grant Colleges—mostly state universities—using a formula based on the number of small farmers in the state. The \$104 million reduction “would be devastating,” says Thomas Fretz, who heads the Northeastern Regional Association of State Agricultural Experiment Station Directors.

Deans at land-grant colleges worry about activities that don’t typically get supported by grants, such as local applications of research. For example, researchers at Colorado State University support the state’s \$200 million potato industry by working with growers to breed resistance to particular diseases during growth or storage. “We are not likely to get

were treated with pI-pC, and cells were analyzed by flow cytometry. The Ly5.2⁺ peripheral lymphocytes from MxCreMcl-1^{fnull} mice were lost within 2 weeks (Fig. 3B); however, the Ly5.1⁺ wild-type BM promoted the survival of the chimeric mice for more than 14 weeks after MxCre-mediated deletion. Liver lysates from pI-pC-treated MxCreMcl-1^{fnull} chimeric mice contained no detectable MCL-1 expression (Fig. 3C). Thus, deletion of *Mcl-1* in the liver is efficient, but nonhematopoietic effects of deletion do not appear to be responsible for the failure of the animals to survive.

Expression of MCL-1 is controlled by growth factor signaling pathways. Both mature lymphocytes and lymphoid progenitors increase expression of MCL-1 in response to interleukin (IL)-7 signaling (13). Stem cell factor (SCF) induces expression of MCL-1 in a human BM-derived cell line (23). To determine whether *Mcl-1* is expressed in response to growth factors in HSCs, we used real-time PCR. The amount of *Mcl-1* mRNA was greater 30 min after exposure of purified HSCs to SCF. IL-6 had a smaller effect, whereas culture with IL-11 did not induce expression (Fig. 4A) (24).

To assess whether *Mcl-1* is required for the survival of cultured BM progenitor populations exposed to growth factors, we used retroviral transduction of Cre into purified BM progenitor populations from *Mcl-1*^{fl/fl} or wild-type mice (25). The purified BM progenitor populations (HSC, CMP, CLP, and GMP) were cultured in appropriate growth factors (26). By 48 hours after retroviral transduction, more than 90% of *Mcl-1*^{fl/fl} Cre-expressing [enhanced green fluorescent protein positive (EGFP⁺)] progenitor cells (HSCs, CMP, and CLPs) were apoptotic (Fig. 4B). Expression of Cre in wild-type BM progenitor populations did not induce apoptosis (Fig. 4B). Therefore, survival of BM progenitors in vitro requires the expression of *Mcl-1* induced by early-acting cytokine signals.

Although previous studies had implicated anti-apoptotic BCL-2 family members in regulating the homeostasis of hematopoietic progenitors (3), our studies indicate that a single anti-apoptotic BCL-2 family member, MCL-1, is essential for promoting the survival of HSC and other hematopoietic progenitors.

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27. We acknowledge C. Beard and E. Williams for technical expertise, J. Fisher for animal husbandry, and E. Smith for editorial assistance. J.T.O. is supported by a postdoctoral fellowship (DRG 1664) from the Damon Runyon Cancer Research Foundation and a Special Fellowship (3421-05) from the Leukemia and Lymphoma Society. This work is supported in part by NIH grant R37CA50239 to S.J.K. and grants DK061320 and CA072009 to K.A.

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Identification of the Sex Pheromone of the German Cockroach, *Blattella germanica*

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The sex pheromone of the German cockroach, *Blattella germanica*, has been characterized as gentisyl quinone isovalerate. This cockroach is a major cause of allergic disease and serves as a mechanical vector of pathogens, making it one of the most important residential and food-associated pests worldwide. The sex pheromone-producing gland in adult females was identified in 1993, but thermal instability of the pheromone made characterization difficult. Now, using a new preparative gas chromatography approach coupled with electroantennographic detection, we have isolated and characterized the pheromone, which we term blattellaquinone, and confirmed the identification by chemical synthesis. The synthetic pheromone was active in behavioral assays and highly effective in field trapping tests, which suggest that it may provide a new tool in cockroach population detection, monitoring, and control.

A sex pheromone that eluded natural product chemists for several decades has been characterized for the German cockroach, *Blattella*

germanica, one of the most important residential and food-associated pests worldwide. Movement of these cockroaches between human and animal waste and food materials allows them to acquire, carry, and mechanically transfer pathogens (1, 2). Moreover, exposure to cockroach-derived allergenic proteins in homes is associated with allergic disease and asthma, particularly in inner-city children (3). Cockroach control, coupled with extensive cleaning, can result in large reductions in cockroach allergens in settled household dust (4-6), but a fundamental constraint in abatement programs has been a lack of effective attractants to lure cock-

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roaches into traps and insecticide baits (7). This deficiency is probably the most important single factor contributing to a continued reliance on scheduled applications of broad-spectrum insecticides to control cockroaches.

A nonvolatile, courtship-eliciting sex pheromone on the female's cuticular surface was previously identified (8), but this pheromone does not have any obvious value in pest control. Based on behavioral and electrophysiological assays, a female sex pheromone that attracts males over some distance, and hence of potential utility in pest control, was discovered in 1993 (9). The pheromone-producing gland was anatomically localized to the pygidium, the last abdominal segment (10), and we observed that virgin females, but not mated females, engage in a characteristic behavior ("calling behavior"), during which they become exceptionally attractive to males (11, 12). Females at this physiological stage are also highly receptive to courting males, and organic solvent extracts of these females specifically attract males, but not adult females or nymphs (9). However, the minute quantity of attractant produced by each female and the thermal instability of the pheromone have hampered efforts to isolate it. Here we report the purification and identification of the pheromone compound, which we accomplished by using a highly sensitive gas-chromatographic-electroantennogram detector (GC-EAD), in which the male cockroach antenna served as a biological detector, and development of a technique for GC purification of a small, thermally unstable sample for nuclear magnetic resonance (NMR) analysis (13).

The pygidia of ~15,000 virgin females were carefully dissected, extracted in dichloromethane, and assayed for attractiveness to males, females, and nymphs in a two-choice olfactometer device (14). We then followed a behaviorally guided chromatographic fractionation of the extract to purify the active fraction. First, the total lipid extract of the pygidia was separated on a silica gel column by eluting successively with mixtures of pentane-ether. The 40% ether fraction, which elicited the highest behavioral responses in males, was subjected to preparative high-performance liquid chromatography (HPLC) purification, and the active fraction was subjected to coupled GC-EAD analysis and GC-mass spectrometry (GC-MS) analysis and further purification using preparative GC (14). GC-EAD analyses of the behaviorally active fractions from preparative HPLC consistently revealed a single EAD-active compound (fig. S1).

The behaviorally active and EAD-active compound was subjected to GC-MS analysis in electron impact (EI) mode (14). It showed a base peak at a mass/charge ratio (m/z) of 57 (100%) and characteristic ions at m/z = 60 (68%), 122 (24%), 138 (16%), 150 (1.7%),

152 (1.3%), 162 (2.7%), 176 (2.0%), 180 (7.1%), 222 (0.9%), and 224 (1.1%). In chemical ionization (CI) GC-MS, the EAD-active compound showed a set of characteristic ions at m/z = 223 (51%), 251 (27%), and 263 (8.9%). Both the EI and CI mass spectra of the natural pheromone indicated a molecular mass of 222 g/mol (EI m/z = 222 and CI m/z = 223), suggesting a number of likely molecular formulas, including $C_{12}H_{14}O_4$, $C_{13}H_{18}O_3$, $C_{14}H_{22}O_2$, $C_{15}H_{26}O$, $C_{15}H_{10}O_2$, $C_{16}H_{14}O$, $C_{16}H_{30}$, and $C_{17}H_{18}$. Fragmentation in the EI mass spectrum gave little

useful information to pare down the number of formulas.

The 600-MHz 1H -NMR spectral data (Fig. 1) supported a $C_{12}H_{14}O_4$ molecular formula. Analysis of chemical shift and coupling data suggested a structure consistent with an isovalerate ester and a *para*-benzoquinone (14). The primary alcohol of *p*-benzoquinone is gentisyl alcohol, and the corresponding quinone is gentisyl quinone (fig. S2). Thus, gentisyl quinone isovalerate was proposed as the structure for the pheromone compound (Fig. 1, inset). Because this is a

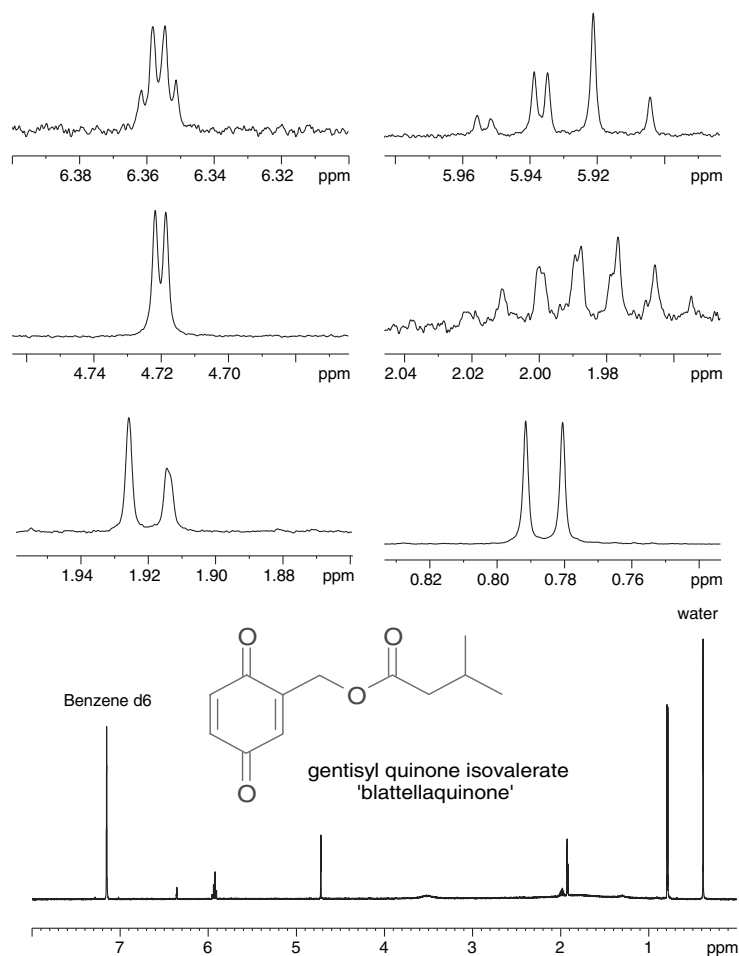


Fig. 1. The 600-MHz 1H -NMR spectrum of the natural pheromone purified by preparative GC. The inset shows the chemical structure of blattellaquinone.

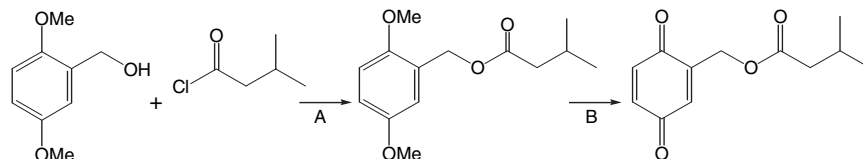


Fig. 2. Scheme for the synthesis of blattellaquinone. Acylation (A) involved addition of isovaleryl chloride to a solution of 2,5-dimethoxybenzyl alcohol, pyridine, and DMAP in CH_2Cl_2 . Excess acid chloride was removed with saturated sodium bicarbonate, and the mixture was extracted with ether, washed with brine, and dried over anhydrous sodium sulfate. The crude ester in acetonitrile was oxidized (B) by adding a solution of $Ce(NH_4)_2(NO_3)_6$ in water. The mixture was extracted with CH_2Cl_2 and redissolved in ether; aqueous sodium bicarbonate was then added, and the ether extract was washed with brine and dried over anhydrous sodium sulfate. See (14) for more details.

previously unknown compound, and there are no recorded chemical shifts of gentisyl quinone esters in deuterobenzene, proof of structure was dependent on chemical synthesis (Fig. 2). The NMR spectrum of the synthetic compound (fig. S3) was found to be identical to that of the natural pheromone (fig. S2). We propose the common name “blattellaquinone” for this pheromone.

The biological activity of synthetic blattellaquinone was compared to that of a crude extract of virgin females in behavioral assays using two-choice olfactometers (14). Males exhibited a clear dose-response to the synthetic pheromone (Fig. 3). More than 60% of the males responded within 1 min by running toward 10 to 100 ng of the pheromone loaded on a filter paper disk. Responding males ran up the olfactometer within 16.4 ± 2.7 s (10 ng) and 8.9 ± 2.2 s (100 ng) of the introduction of the pheromone. When making a choice between 100 pg of synthetic blattellaquinone and a solvent control, $93.8 \pm 6.2\%$ of 53 responding males chose the pheromone. This is similar to the percentage of males ($92.5 \pm$

2.1% of 244 males) that chose the crude dichloromethane extract of one virgin female over a solvent control. However, at high doses (10 and 100 μg), we observed that many males became disoriented as they approached the pheromone, and only $52.3 \pm 7.2\%$ (of 55 responsive males) and $68.6 \pm 9.6\%$ (of 53 responsive males), respectively, chose the pheromone. These observations suggest that precise doses and careful formulations will be required to optimize the efficiency of this pheromone in pest control.

Field tests of blattellaquinone were performed in a cockroach-infested pig farm. Whereas nymphs and adult females did not respond at any dose of the pheromone between 0 and 1 mg, adult males exhibited a clear dose-response in their behavioral attraction to pheromone-baited traps (Fig. 4). These results confirm that blattellaquinone is a female sex pheromone of *B. germanica* that specifically attracts conspecific males.

Substituted benzoquinone compounds are ubiquitous animal and plant excretions and are most commonly used as defensive secretions

and feeding deterrents (15). Quinone-containing defensive compounds have been identified in some cockroaches (16). It is possible, therefore, that blattellaquinone also served a defensive function in *B. germanica* and was co-opted to play a role in sexual communication, as have some other multifunctional semiochemicals (e.g., cuticular hydrocarbons serve in waterproofing as well as in sexual and nestmate recognition in some insects). Our preliminary observation that only nanogram amounts of this compound are stored by females suggests, however, that blattellaquinone probably no longer functions in defense. It will be important to determine whether this compound occurs in immature cockroaches and in adult males, although organic solvent extracts of these stages fail to attract males (9).

The identification of blattellaquinone as the sex pheromone of *B. germanica* culminates a long and arduous search for a volatile attractant in this important pest species. It now offers new options in cockroach population control and allergen mitigation.

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Supporting Online Material

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 Materials and Methods
 Figs. S1 to S3
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Fig. 3. Behavioral responses of male *B. germanica* to one female equivalent of a crude dichloromethane extract and to various doses of blattellaquinone. The pheromone was applied in 5 μl of dichloromethane to a filter paper disk and presented to single males acclimated in the two-choice olfactometer versus a dichloromethane-treated control filter paper disk. Behavioral response is defined as quiescent males that were stimulated to run out of their cages within 60 s. Each assay block consisted of testing 10 to 16 males in individual olfactometers and means \pm SEM were calculated from 3 to 18 blocks of assays. The inset shows a male German cockroach responding to blattellaquinone emanating from a filter paper disk.

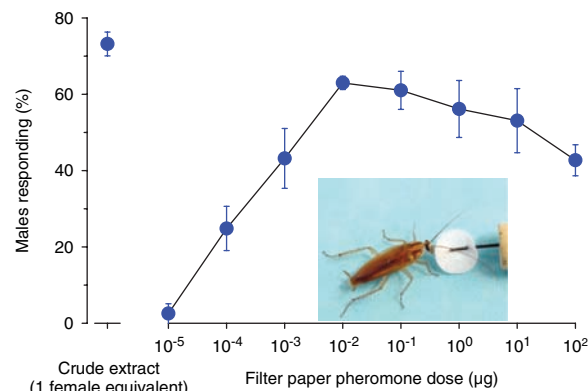


Fig. 4. Trap catches of *B. germanica* using various doses of the synthetic pheromone, blattellaquinone. The pheromone was applied in 50 μl of dichloromethane to a 5-mm sleeve-type rubber septum, which was hung inside a 1-pint (~470 ml) wide-mouth mason jar whose inside wall was treated with a thin layer of petroleum jelly (to prevent trapped cockroaches from escaping). Seven treatments were placed in a completely randomized Latin square design along five walls of a cockroach-infested pig farm, and treatments were rotated daily so that all positions along the wall received all seven treatments over seven consecutive nights (i.e., 35 replicates per dose). Data were log-transformed and analyzed by multiway analysis of variance, followed by Fisher’s least significant difference mean separation (17). An independent trial (not shown) extended the dose-response using three treatments (0, 1, and 10 mg) along seven walls (21 replicates per dose); there were no significant differences between 1- and 10-mg doses.

